REMARKS

Reconsideration and withdrawal of the rejections of the claimed invention is respectfully requested in view of the amendments, remarks and enclosures herewith, which place the application in condition for allowance.

I. STATUS OF CLAIMS AND FORMAL MATTERS

Claims 1, 3 and 5-21 are pending in this application. As the response is to a final rejection, the applicants present that the amendment to claim 1 should be entered as it would serve to narrow the issues for appeal (e.g. scope of the crosslinked hydrophilic polymers and the range by weight of glycerol as plasticizer), reduces the number of claims to be appealed (claim 2 is cancelled) and presuming that a proper search was made, does not raise any new issues which require further search or consideration.[1] No new matter has been added by this amendment.

The applicants have made the amendment to claim 1 to expedite prosecution. However, entry of the amendment would not be required to proceed to Appeal for the reasons cited below.

It is submitted that the claims, herewith and as originally presented, are patentably distinct over the prior art cited in the Office Action, and that these claims were in full compliance with the requirements of 35 U.S.C. § 112.

II. THE 35 U.S.C. 103(a) REJECTION HAS BEEN OVERCOME

A. Claims 1, 2, 4, 6, 7, 9, 13-18, 20 and 21 were rejected as allegedly being obvious over Becher (U.S. Patent 6,153,222) in view of Zerbe et al. (U.S. Patent 6,177,096 – "Zerbe").

B. Claims 3 and 5 were rejected as allegedly being obvious over Becher (U.S. Patent 6,153,222) in view of Zerbe et al. (U.S. Patent 6,177,096 – "Zerbe"), further in view of Mulye (U.S. Patent 6,946,146).

C. Claims 1, 2, 9, 13-19 and 21 were rejected as allegedly being obvious over Becher (U.S. Patent 6,153,222) in view of Lydzinski et al. (U.S. Patent Application Publication 2003-0099692 – "Lydzinski").

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[1] It is noted that MPEP 904.02 (General Search Guidelines) states in part that "In the examination of an application for patent, an examiner must conduct a thorough search of the prior art….The search should cover the claimed subject matter and should also cover the disclosed features which might reasonably be expected to be claimed." The reference to "in-situ" can be found in paragraphs [0013], [0014] and [0053] of the publication of the specification (US 2007-0071796)

As these rejections all utilize the Becher reference as a primary reference, the response to the above rejections are addressed collectively below.

1. Arguments presuming entry of the amendment

As reiterated by the Supreme Court in *KSR International Co. v. Teleflex Inc. (KSR)*, 550 U.S. 398, 82 USPQ2d 1385 (2007), the framework for the objective analysis for determining obviousness under 35 U.S.C. 103 is stated in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966). Obviousness is a question of law based on underlying factual inquiries. The factual inquiries enunciated by the Court are as follows:

(A) Determining the scope and contents of the prior art;
(B) Ascertaining the differences between the prior art and the claims in issue;
(C) Resolving the level of ordinary skill in the art; and
(D) Evaluating evidence of secondary considerations.

When ascertaining the differences between the prior art and the claims in issue, both the claimed invention and the prior art are considered as a whole.

Once the *Graham* factual inquiries are resolved, Office personnel must determine whether the claimed invention would have been obvious to one of ordinary skill in the art.

The applicants maintain their position from their previous response which is commented on and reproduced further below. In addition, the claimed dosage film form now requires ---in-situ crosslinked hydrophilic polymers---.

As a result of the in-situ crosslinking of the film-forming hydrophilic polymers, it is possible to ensure sufficiently secure handling of the dosage form in film form, e.g. removal of the dosage form from the package and application to the surface of a living creature can be now be accomplished without damaging the dosage form by tearing.

The crosslinking also makes it possible according to the invention to provide dosage forms in film form with minimum tear strength of 40 N to at least 60 N (see examples 5 to 7). This in-situ crosslinking of the film-forming layer based on hydrophilic polymers preferably takes place during formation of the layer with the aid of known crosslinkers [0014].

However, when considering the references as a whole and the many possible permutations of possible inventions represented by the collective teachings of Becher, Zerbe, Mulye and Lydzinski. do not render the applicants' claimed invention to be obvious.

Becher refers to the use of crosslinked polymers like carboxyvinyl copolymers (e.g. AquaKeep®) and/or crosslinked polyvinyl pyrrolidone (e.g. Kollidone® 90) as film formers in combination with glycerol as softener carboxyvinyl copolymers is a super absorbent polymer based on polyacrylate. Polyvinylpyrrolidone (PVP) is a water-soluble polymer made from the monomer N-vinylpyrrolidone (col. 2, lines 34-39, 56-63). Becher is characterized in the Office Action as merely lacking a teaching of the amount of glycerol based on the total amount of crosslinked hydrophilic polymer.

However, Becher does not teach the use of crosslinked ***hydrophilic*** polymers and as acknowledged in the Office Action, Becher only refers to glycerol as part of a "further substance" which includes the broad class of compounds such as fillers, active substances, foamers, film formers, flavoring agents, softeners and sweeteners, i.e. even if Becher had taught crosslinked hydrophilic polymers, Becher would not have directed one of ordinary skill in the art to a combination of glycerol with in situ crosslinked hydrophilic polymers.

Zerbe refers to film forming ***non-crosslinked*** polymers comprising preferred water-soluble polymers selected from water-soluble cellulose derivates and polyacrylates, among others and one or more plasticizers or surfactants and one or more polyalcohols (col. 2, line 32-36). Glycerol is mentioned as an example of a polyalcohol (col. 3, line 10-15). The references teach 20 % of glycerol based on the total amount of the hydrophilic polymer, but not of the crosslinked hydrophilic polymer.

In contrast, the claim 1 as amended now refers to 30% - 60% glycerol content (which was originally part of dependent claim 2). which is not suggested by Zerbe and like Becher, only mentions glycerol in the context of broad classes of optional ingredients ("..the formulation may contain a combination of certain plasticizers or surfactants, colorants, sweetening agents, flavors, flavor enhancers, or other excipients commonly used to modify the taste of formulations intended for application to the oral cavity.")

Mulye refers to a composition coated onto the core containing a drug in an oral unit dosage form, ***such as a tablet, capsule, pill, granule or powder to form*** the desired preparation (col. 11, line 63-64). Mixtures were compressed using a tablet press (see Examples). Therefore, the Mulye does not teach dosage form in film form or at the very least provide no specific

direction to film forms such that inclusion of film forms would also include virtually an infinite number of other possible forms.

The plasticizer may be selected from those plasticizers normally used in coating compositions of pharmaceutical e.g. glycerol and may be present in the coating in amounts ranging from about 0.01% to about 25% by weight and more preferably from about 5 to about 15% by weight based on the dry weight of the coating (col. 8, line 63-64).

Lydzinski refers to an oral film containing chemically modified starch which has been e.g. crosslinked. Plasticizers may be added to increase the apparent flexibility of the film particularly in an amount of about 15 % by weight of the starch component (page 2 [0026]). Potential plasticizers, among others include polyols. Glycerol is only mentioned as an example for polyesters (Glycerin Triacetat).

None of the documents individually or collectively teaches using an active ingredient comprising layer based on in-situ crosslinked hydrophilic polymers. Even though it is known from the prior art using glycerol up to 20% by weight to increase the apparent flexibility of the film our invention involves an inventive step to incorporate large amount of glycerol into the active ingredient containing layer by using in situ crosslinked hydrophilic polymers to achieves the necessary improvement in plasticity.

The allegation that the weight range of 30% to 60% by weight could be obtained by routine optimization is refuted for two reasons.

First, the Office in general often refers to *In re Aller*, but do not consider the very next section in the MPEP, i.e. MPEP 2144.05 section II.B. (Optimization of Ranges) states that "A particular parameter must first be recognized as a result-effective variable, i.e., a variable which achieves a recognized result, before the determination of the optimum or workable ranges of said variable might be characterized as routine experimentation. *In re Antonie*, 559 F.2d 618, 195 USPQ 6 (CCPA 1977)." Nothing within Becher, Zerbe, Mulye and Lydzinski recognized glycerol content as a results effective variable within the context of their own inventions and certainly not in the context of the applicants' claimed invention.

Second, plasticizers are normally employed in an amount of up to 20% by weight based on the amount of polymer. When the percentage amounts of plasticizer are relatively high, phase

separations may occur, e.g. due to crystallization, so that the films are no longer transparent and their physical properties such as the tear strength are adversely affected.

With regard to consideration of the prior art as a whole, the current rejection resembles that of an improper scavenger hunt whereby the claimed elements are simply collected without any consideration of invention or the respective teachings of the reference as a whole. However, the applicants' invention is not each claim element in isolation, but the simultaneous presence of each of the elements of claim 1 which the combination of Becher, Zerbe, Mulye and Lydzinski never teaches. In fact, one of ordinary skill in the art presented with all the possible elements described within the specification of Becher, Zerbe, Mulye and Lydzinski would be overwhelmed by the infinite number of possible permutations of products which could be obtained by mixing and matching random elements from within Becher, Zerbe, Mulye and Lydzinski specification and would not have arrived at the applicants' claims without having them before him as an "answer key".

Lastly, while the applicants argue that all of the claims are unobvious over the combination of Becher, Zerbe, Mulye and Lydzinski, the applicants also note that the dependent claims appear to have been taken in isolation for the specific element and not for all of the elements which are represented in the dependent claim. A representative example was the statement on page 6, lines 17-19 which stated "With respect to the weight range of the plasticizer in present claims 1, 2 and 21, Lydzinski teaches using plasticizers up to about 15% by weight an further indicates that any desired amount may be employed."

However, claim 21 is dependent on claims 20 which in turn is dependent on claim 18, which in turn is dependent on claim 17, which in turn is dependent on claim 16 and which is now dependent on claim 1 as amended, i.e. even if the 15% by weight element of claim 21 had been taught by Lydzinski, it still does not account for the four additional elements simultaneously present in claim 21 (i.e. the elements of claims 16, 17, 18 and 20).

2. Arguments presuming non-entry of the amendment

The applicants' arguments above, with the exception to those made in view of "in-situ" crosslinking are also applicable here.

(Arguments from previous response)

When making the determination of obviousness, both the applicants' claimed invention and the cited references must be considered as a whole.

The applicants' claimed invention is clearly directed toward a dosage form in film form for surface administration. Moreover, the film form of claim 1 has 20% to 60% by weight of glycerol as plasticizer. As noted in the applicants' specification, the state of the art for these types of dosage forms was that in order to have proper elasticity, softness and flexibility, the amount of plasticizers employed was up to 20% by weight based on the amount of polymer (see paragraph [0008] of the publication of this application).

One of ordinary skill in the art would have expected that using greater amounts of plasticizers would have resulted in phase separations due to crystallization resulting in films which are not transparent and/or having the plasticizer separate out of the film (see paragraph [0009] of the publication of the application).

a. Becher and Zerbe do not contradict the state of the art with respect to plasticizers

With respect to Becher, there is nothing within the specification which would contradict the state of the art presented by the applicants in their application. Becher does not refer to the use of plasticizers (the term is nowhere to be found in Becher). Becher does refer to glycerol as a softener under the heading of "Further Substances", but one of ordinary skill in the art would not have considered glycerol to be a required element of the invention or that using 20% or more of glycerol would not have resulted in phase separations due to crystallization.

The Zerbe reference does not remedy the deficiencies of Becher and is directed to a different invention, i.e. Becher's polymers are crosslinked, but Zerbe's are not. As such, there was no reasonable expectation of success that the amount of plasticizer used by Zerbe would have been applicable to the invention of Becher especially when both Becher and Zerbe refer to plasticizers as being optional elements.

Mulye is relied upon only for the teaching of a polymeric film and Lydzinski is relied upon only for the teaching of the use of different active ingredients and as such do not remedy the deficiencies of the combination of Becher and Zerbe as applied to claims 1, 2, 4, 6, 7, 9 and 13-15.

Therefore, the applicants claims are unobvious over any combination of Becher, Zerbe, Mulye and/or Lydzinski as elements of the applicants claimed dosage form are not taught to be used in combination.

b. Applicants have shown evidence of unexpected results

Consideration of obviousness also requires a consideration of any evidence of unexpected results. For the presently claimed invention, a required element of the invention is that the plasticizer is glycerol. Whereas the embodiments of the applicants claimed invention using glycerol as plasticizer show easy handleability and applicability to the human skin and mucous membrane, this was not true of comparative examples where no plasticizer was used (Comparative Example 1) or alternative plasticizers were used (polyethylene glycol (Comparative Example 2); sorbitol (Comparative Example 3); and triethyl citrate (Comparative Example 4)).

As such, the applicants claims are also unobvious because the applicants have surprisingly shown that the specific use of glycerol as a plasticizer allows one of ordinary skill in the art to be able to use more plasticizer than was previously thought possible by those of skill in the art.

D. Claims 1, 2 and 6-21 were rejected as allegedly being obvious over Carli et al. (U.S. Patent 5,582,836 – "Carli") in view of Lydzinski et al. (U.S. Patent Application Publication 2003-0099692 – "Lydzinski").

1. Arguments presuming entry of amendment

As reiterated by the Supreme Court in *KSR International Co. v. Teleflex Inc. (KSR)*, 550 U.S. 398, 82 USPQ2d 1385 (2007), the framework for the objective analysis for determining obviousness under 35 U.S.C. 103 is stated in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966). Obviousness is a question of law based on underlying factual inquiries. The factual inquiries enunciated by the Court are as follows:

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Once the *Graham* factual inquiries are resolved, Office personnel must determine whether the claimed invention would have been obvious to one of ordinary skill in the art.

The applicants maintain their position from their previous response which is commented on and reproduced further below. In addition, the claimed dosage film form now requires ---in-situ crosslinked hydrophilic polymers---.

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However, when considering the references as a whole and the many possible permutations of possible inventions represented by the collective teachings of Carli and Lydzinski. do not render the applicants' claimed invention to be obvious.

The claims were alternatively rejected over Carli and Lydzinski, but this is essentially a duplicate rejection of the Becher rejections referred to above with the same attendant problems, i.e. Carli refers to a cross-linked dosage form whereas Lydzinski does not (uses starch products) and does not contradict the state of the art with respect to the use of plasticizers.

2. Arguments presuming non-entry of the amendment

The applicants' arguments above in section C. 1 and D. 1, with the exception to those made in view of "in-situ" crosslinking are also applicable here.

(Arguments from previous response)

The claims were alternatively rejected over Carli and Lydzinski, but this is essentially a duplicate rejection of Becher and Zerbe with the same attendant problems, i.e. Carli refers to a

cross-linked dosage form whereas Lydzinski does not (uses starch products) and does not contradict the state of the art with respect to the use of plasticizers.

Carli is an even weaker reference as not only does it fail to mention the use of plasticizers, it also fails to even mention the use of glycerol in any context. Moreover, there is no evidence that Lydzinski' reference to "any desired amount" would have been in amounts greater than that thought possible by those of skill in the art (the fact that Lydzinski referred to ranges consistent with the state of the art, i.e. 0 to 15% and 0 to 10%, suggests otherwise) or that Lydzinski's ranges would have been applicable to crosslinked hydrophilic polymers.

In addition, the combination of Carli and Lydzinski does not teach the unexpected results which are achieved by the specific use of glycerol as a plasticizer.

Therefore, the combination of Carli and Lydzinski also does not render the applicants claimed dosage form to be obvious.

CONCLUSION

In view of the remarks and amendments herewith, the application is believed to be in condition for allowance. Favorable reconsideration of the application and prompt issuance of a Notice of Allowance are earnestly solicited. The undersigned looks forward to hearing favorably from the Examiner at an early date, and, the Examiner is invited to telephonically contact the undersigned to advance prosecution.

Respectfully submitted,
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